

## **Therapy: Current Status of Oral Rehydration**

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Therapy for enteric infections has been anchored on the success of oral rehydration. Although the global use of ORT is limited to approximately 50% of the need, three million lives are saved annually. In addition to the invaluable role for ORT in replacing fluid loss during childhood diarrhea, ORT is finding an increasingly important application in geriatric care.

The origin of ORT lay in balance studies, the understanding of solute-mediated transport, and the use of digestible polymers that increased co-transport without incurring an osmotic cost. An essential element in the development of ORT were studies on cholera patients undertaken at the Cholera Research Laboratory now the International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B) in Dhaka, and the Johns Hopkins ICMRT, Calcutta, India. The basis of ORT was the observation that providing glucose with water and salts greatly enhanced the uptake of water and solutes, and even though diarrhea continued unabated, the net result was a positive fluid balance. Standard glucose-based ORT replaces lost volume, but does not reduce diarrhea. The cotransport of sodium and glucose provides the means to replace fluid losses during intestinal inflammation or intoxication. The use of rice-based ORT increases efficiency of fluid absorption because starch, when digested, provides more glucose to intestinal cotransport sites at low osmotic pressure in the lumen.

There remain opportunities to improve ORT by adding proteins or peptides that could hasten recovery of intestinal epithelium while providing added cotransporting channels. In addition, additives could be included to reduce the quantity of diarrhea, decrease inflammation, or inhibit microbial pathogenesis. In addition, improving the taste of ORT would encourage more widespread adoption. Criteria for additives to ORT must include non-toxicity in high doses, low price, and broad accessibility. In addition, the taste should not detract from the acceptability of ORT, or work against the long-term efforts at advocacy for this remarkable therapy. Potential additives include zinc, histidine or glutamine containing proteins or peptides, lactoferrin, lysozyme (breast milk proteins), and gut flora restoratives.

ORT will play an increasing role in geriatric medicine. The case fatality rate from gastroenteritis increases steadily with age, reaching over 100 deaths per 10,000 hospitalizations. The elderly have a high risk from the complications of hypovolemia, due to a diminished circulatory reserve, blockage of arteries to vital organs, lowered thirst drive, reduced mobility and balance, diuretics and low salt diets, and the effects of drugs used to lower blood pressure. ORT remains a potent accessible and low-cost treatment that satisfies the essential replacement concept: to put back what is lost in quantity and composition. Nonetheless, the following research needs remain outstanding:

- Identify the maximum co-transporting substrates with the lowest osmolarity
- Identify the most effective additives
- Improve the taste of ORT
- Explore adjuvant effects that may improve response to oral vaccine or natural infection

- Development of K<sup>+</sup> free ORT to minimize the risk of hyperkalemia in renal failure
- Maintain low cost and continue to advocate broader usage to reach the 50% who presently do not benefit from this remarkable treatment option.